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(54) Title: METHOD FOR SCREENING FOR ANTI-AMYLOIDOGENIC PROPERTIES AND METHOD FOR TREATMENT OF NEURODEGENERATIVE DISEASE

(57) Abstract: The methodologies of the present invention demonstrate that a critical balance between pro- and anti-amyloidogenic molecules exists that regulates amyloid formation and cell death in Alzheimer's disease and Parkinson's disease. β-Synuclein, the non-amyloidogenic homologue of α-synuclein, is a negative modulator of α-synuclein and Aβ aggregation, having neuroprotective properties against α-synuclein and Aβ neurotoxicity and that β-synuclein and therapeutic agents derived therefrom block amyloidogenesis and neurodegeneration *in vivo*. The method of the present invention establishes that β-synuclein blocks Aβ aggregation either by direct inhibition of Aβ amyloidogenesis or indirectly via either α-synuclein or its 35 a.a. NAC region, inferring neuroprotective characteristics within the effected cells. The generation of a transgenic mouse line and a cell-free system overexpressing α-synuclein characterizes the mechanisms by which β-synuclein blocks α-synuclein and Aβ aggregation and that this mechanism offers protection to the cell against amyloid formation as seen in the pathologies of Alzheimer's disease and Parkinson's disease.

INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :G01N 33/00; A01K 67/00; C12Q1/02

US CL :800/3, 12; 435/29; 514/1, 44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 800/3, 12; 435/29; 514/1, 44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST, CAPLUS, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GOLDBERG, M.S. et al. Studies of Human α-Synuclein in Transgenic Mice. Society for Neuroscience Abstracts. 1999, Vol. 25, No. 1-2, pp. 2055, see lines 6-20.	1-11
X --- Y	MUCKE, L. et al. Potential Roles of α1-antichymotrypsin and α-synuclein in Alzheimer's Pathogenesis Assessed in Bigenic Mice Expressing Human Amyloid Precursor Proteins. Society for Neuroscience Abstract. 199, Vol. 25, No. 1-2, pp. 302, see lines 4-21.	1 and 2 -- 3-18
Y	COLE, G. M. et al. Amyloid-Associated α-Synuclein (NACP) Pathology in Aged Amyloid Precursor Transgenic Mice. Society for Neuroscience Abstracts. 1999, Vol. 25, No. 1-2, pp. 298, see lines 7-19.	1-11

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HASHIMOTO, M. et al. Human Recombinant NACP/α-Synuclein is Aggregated and Fibrillated In Vitro: Relevance for Lewy Body Disease. Brain Research. 1998, Vol. 799, No. 2, pp. 301-306, see pages 303-305.	1-11 and 19-21
P	TAKEDA, A. et al. Abnormal Accumulation of NACP/α-Synuclein in Neurodegenerative Disorders. American Journal of Pathology. Vol. 152, No. 2, pp367-372, see pages 367-371.	1-11and 18-21
Y	JENSEN, P. H. et al. Binding of A/β to α- and β-Synucleins: Identification of Segments in α-Synuclein/NAC Precursor that Bind Aβand NAC. Biochemistry Journal. 1997, Vol. 323, pages 539-546, see especially pages 541-545.	19-21